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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,342	05/26/2000	YUKIO KATO	046124-5025	3974

9629 7590 06/09/2006

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,342	KATO ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,17,25,27,32 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17,25,27,32 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/08/06 has been entered.

Applicant added new claim 40, which is related to claims 15, 17, 25, 27, 32, and is not new matter.

Accordingly, claims 15, 17, 25, 27, 32 and 40 are being examined.

NEW REJECTIONS BASED ON NEW CONSIDERATION

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 recites the limitation ""the nucleic acid" in claims 15, 17. There is insufficient antecedent basis for this limitation in the claims 15 and 17, which do not recite "a nucleic acid".

This rejection could be obviated by amending claim 32 to recite, for example, "comprising one of the DNAs of claims 15 and 17, or one of the nucleic acids of claims 25 and 27".

Claim Rejections - 35 USC § 101, Utility

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 15, 17, 25, 27, 32 and 40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

Claim 15 is drawn to: An isolated DNA encoding a protein having SEQ ID NO:2.

Claim 17 is drawn to: An isolated DNA having the nucleotide sequence comprising nucleotides 49 to 3,183 of SEQ ID NO:1.

Claims 25, 27 are drawn to: An isolated nucleic acid molecule consisting of SEQ ID NO:1 (claim 25), or the complete full length complement of SEQ ID NO:1 (claim 27).

Claim 32 is drawn to: A kit for distinguishing a differentiated chondrocyte from a dedifferentiated chondrocyte comprising one the nucleic acids of claims 15, 17, 25 and 27.

Claim 40 is drawn to: An isolated DNA which hybridizes under stringent conditions with a nucleotide sequence ranging from the 49th to 3,183rd bases of SEQ ID NO:1, wherein the stringent conditions comprise a temperature in the range of that from the Tm of a hybrid of completely matching nucleic acids to a temperature 20^0 C lower than the Tm, and the DNA encodes a protein specifically expressed in differentiated chondrocytes.

The specification asserts that the CDEP polynucleotide SEQ ID NO:1 is a new member of the Rho GEF(guanine nucleotide exchange factor) family, wherein Rho GEF, by dissociating GDP from Rho, activates the Rho protein, a protein having important role in controlling cell adhesion, diffusion, migration, proliferation and differentiation (p.12). The assertion that SEQ ID NO:1 and the encoded protein thereof belong to the Rho GEF family is only based on sequence similarity of the domains, DH and erzin-like, of the protein encoded by SEQ ID NO:1 and the common domains known for members of the Rho GEF family. The specification states that it is well known that the DH-PH domain of proteins of the Rho GEF family is necessary for Rho GEF activity (p.11, last paragraph), and that the protein encoded by SED ID NO:1 has DH domain which is about 22% similar to the DH domain of the protein Dbl, Ost, or Ect2 of the oncogene Rho GEF family, and 25% similar to that of FGD1, a causative gene for faciogenital dysplasia (p.11, first paragraph). The specification speculates that DH and PH domain of the CDEP protein encoded by SEQ ID NO:1 thus may perform GDP-GTP exchange reaction to regulate the activity of Rho, and that CDEP protein encoded by SEQ ID NO:1 is considered to be an activator of Rho (p.22, last paragraph, bridging p.23). The specification also states that the CDEP polypeptide encoded by SEQ ID NO:1 has an erzin-like domain which is 27% similar to ezrin domain of ezrin protein, and 43 % similar to that of band 4.1 known in the art (p.10, second paragraph). The specification speculates that said ezrin-like domain of SEQ ID NO:1 may dissociate Rho inhibitor from Rho (p.11, lines 15-18, and p.22, last paragraph).

It is noted that one cannot determine that the claimed domains of SEQ ID NO:1 are essential for and confer the property of activating Rho protein, based solely on sequence or domain similarity for the following reasons. Although the specification aligns and compares the

amino acid sequences of the claimed domains with the domains erzin, and DH known in the art (the instant figures 3-4), there is no disclosure in the specification, or in the art that the conserved amino acid residues among the different domains known in the art are consensus sequences, which consensus sequences confer and are required for the common activity of the domains erzin, or DH known in the art. There is no disclosure in the specification that the claimed domains contain the consensus sequences of the domains known in the art. The specification only states that there are some percentages of similarity between the claimed domains and the domains known in the art. However, it is clear that, although the CDEP protein encoded by SEQ ID NO:1 has 1) a domain which is only 27% similar to ezrin, and only 43 % similar to band 4.1 known in the art (p.10, second paragraph), and 2) a DH domain which is only 22% similar to Db1, Ost, Ect2 of the oncogene Rho GEF family, and only 25% similar to FGD1, there is a 73%, 57%, 78% and 75% dissimilarity between the domains of SEQ ID NO:1 and the corresponding domains of erzin, band 4.1, Db1, and FGD1, respectively, and the effects of these dissimilarities upon protein function cannot be predicted, in view of the unpredictability of protein chemistry, as taught by Bowie, Burgess et al, and Lazar et al, all of record. Further, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein or motifs thereof found in the sequence databases. For example, Ofran Y et al, 2005 (Drug Discovery Today, 10 (21): 1475-1482), in a review of methods for predicting protein-function by homology, teach that homology based prediction of a protein function (homology-based annotation transfer) is one of the main source of incorrect functional annotations that occur in databases, and is inaccurate and limited, and that the function of only less than 35% of all proteins could be predicted automatically, when accepting errors of less than or equal 5%

(p.1476, second column, item under "Drug discovery and protein-function prediction, and p.1478, first column, last paragraph, under "Although powerful, homology-based transfer is inaccurate and limited", bridging second column). Skolnick et al, 2000 (Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork, 2000 (Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Similarly, Barlett et al, 2003 (In: Structural Bioinformatics, Bourne et al, eds, Wiley-Liss, Inc., pages 387-407) teach that it is not always that family members will have related functions, as shown by the classic example of divergence of function within the homologous family of lysozyme and alpha-lactalbumin, and as shown by the diverse function of 31 enzyme superfamilies (p.395, item under "Homologous families and function", and p.397, first paragraph). Barlett et al further teach that when structure motifs are used for predicting protein function, such as in the case of enzymes, detailed knowledge of the active site is required (p.399, last paragraph). Rost et al, 2003 (Cell Mol Life Sciences, 60: 2637-2650) teach that using sequence homology to predict protein function is problematic and limited in scope (abstract, p.2641). Rost et al further teach that using known sequence motifs for predicting function is not always successful, because of the difficulty in predicting structure around the site, and considerable variation of consensus sequences, as for the case of phosphorylation site and kinase substrate specificity, respectively (p.2643, first column, last paragraph). In the instant application, the specification does not teach whether there are

consensus sequences required for the activity of the known domains erzin, and DH of proteins of the family Rho-EGF (see figures 3 and 4 of the instant application), and that the claimed domains contain these consensus sequences, nor the structure around the site. Thus, in view of a lack of sufficient disclosure in the specification, and further in view that structural similarity, or domain similarity cannot be predictably used for predicting a protein function, one cannot determine at the time the invention was made that the protein encoded by SEQ ID NO:1 activates the Rho protein, and further experimentation is required to determine what use is for the claimed sequence. Thus, neither the specification nor any art of record teaches what the claimed polynucleotide of SEQ ID NO:1 and the encoded polypeptide thereof are, what they do; they do not teach a relationship to any specific diseases or establish any involvement in the etiology of any specific diseases.

In the absence of any disclosed relationship and the lack of correlation between the claimed CDEP polynucleotide and the encoded polypeptide thereof and any disease or disorder, and further in view that any potential diagnostic or therapeutic utility is not yet known and has not yet been disclosed, the utility is not substantial. Further research is necessary to determine what use is for the claimed polynucleotide or the encoded polypeptide thereof. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPO at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. 101.

Further, in a **post filing** submitted reference by Koyano et al, 2001 (Osteoarthritis and Cartilage, 9, Suppl A, S64-S68), although an N-truncated CDEP protein, which contains the DH and PH domain, has an constitutive activity of guanine nucleotide exchange, and activates the

Rho protein (figure 4B and p. S66, first column, paragraph under GEF activity of CDEP for RHO in vitro), it is not clear whether the CDEP protein cited in Koyano et al is the same as the CDEP protein encoded by SEQ ID NO:1 of the instant claimed invention. Further, even if the CDEP protein cited in Koyano et al is the same as the protein encoded by SEQ ID NO:1, the teaching by Koyano et al is post-filing data, thus further confirms that further experimentation was required at the time the invention was made to determine what use is for the claimed SEQ ID NO:1.

It is further noted that encoding a protein that specifically expresses in differentiated chondrocytes is not a critical function of SEQ ID NO:1, which function distinguishes the claimed CDEP polynucleotide from others, because there are unrelated sequences that are also specifically expressed in differentiated chondrocytes (see, for example, Iwamoto M et al, 2001, Osteoarthritis and Cartilage, 9 Suppl A: S41-7; Kolettas E et al, 1995, J Cell Science: 108 (Pt 5): 1991-9; Doege KJ et al, 1994, JBC, 269(46): 29232-29240).

For reasons set forth above, the disclosure satisfies none of the three criteria of a specific, substantial, and credible utility. *See In re Kirk*, 153 USPO 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed CDEP polynucleotides. Because the claimed CDEP polynucleotides are not supported by a specific, substantial asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

Claim Rejections - 35 USC § 112 First Paragraph, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 17, 25, 27, 32 and 40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 40 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) 40 contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 40 is drawn to: An isolated DNA which hybridizes under stringent conditions with a nucleotide sequence ranging from the 49th to 3,183rd bases of SEQ ID NO:1, wherein the stringent conditions comprise a temperature in the range of that from the Tm of a hybrid of completely matching nucleic acids to a temperature 20^0 C lower than the Tm, and the DNA encodes a protein specifically expressed in differentiated chondrocytes.

It is noted that it is well known in the art that each 1^0 C difference with the calculated Tm represents 1% mismatch (Sambrook et al, eds, 1989, Molecular Cloning, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, p.11.52, item 3). Thus "hybridizing at a temperature in the range of that from the Tm of a hybrid of completely matching nucleic acids to a temperature 20^0 C lower than the Tm" would allow hybridization of sequences that are at least 80% similar to SEQ ID NO:1.

The claim 40 encompasses a genus of CDEP variants of SEQ ID NO:1 having at least 80% similarity with SEQ ID NO:1, with unknown structure and function.

Since one cannot predict that the claimed domains of the protein encoded by SEQ ID NO:1 are essential for and confer the property of activating Rho protein, supra, and since encoding a protein specifically expressed in differentiated chondrocytes is not a critical function of SEQ ID NO:1, **there is no correlation between structure and the critical function of SEQ ID NO:1**. Further, since the claim encompasses a genus of CDEP variants with unknown structure and function, **the recited single DNA, SEQ ID NO:1, is not a representative species**.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc.,

296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

In this case, the specification does not describe the claimed genus of CDEP DNAs, that hybridize to SEQ ID NO:1 under the stringent conditions recited in claim 40, in a manner that satisfies either the standards as shown in the example of Lilly or Enzo. The specification does not provide sufficient structure or common structure, other than a single polynucleotide, SEQ ID NO:1, to support the broad breath of the claimed genus. Nor is there any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single polynucleotide, SEQ ID NO:1, this does not provide a description of the claimed genus of DNAs that would satisfy the standard as shown in the example of Enzo.

The specification also fails to describe the claimed genus of CDEP DNAs, by the standards shown in the example in Lilly. The specification describes only a single polynucleotide, SEQ ID NO:1. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features

common to the members of the genus, which features constitute a substantial portion of the genus."

The specification does not provide an adequate written description of the claimed genus of CDEP DNAs, that is required to practice the claimed invention. Thus, the specification does not meet the 112, first paragraph written description requirement, and one of skill in the art would reasonably conclude that Applicant did not have possession of the claimed genus of CDEP DNAs at the time the invention was made.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 40 is rejected under 35 U.S.C. 102(e) as being anticipated by Studier (US 5,407,799, filed on 04/18/1995).

Claim 40 is drawn to: An isolated DNA which hybridizes under stringent conditions with DNA having a nucleotide sequence ranging from the 49th to 3,183rd bases of SEQ ID NO:1, wherein the stringent conditions comprise a temperature in the range of that from the Tm of a hybrid of completely matching nucleic acids to a temperature 20^0 C lower than the Tm, and the DNA encodes a protein specifically expressed in differentiated chondrocytes.

It is noted that the limitation of "the DNA encodes a protein specifically expressed in differentiated chondrocytes" is reasonably interpreted as the property of the DNA having a nucleotide sequence ranging from the 49th to 3,183rd bases of SEQ ID NO:1".

It is further noted that it is well known in the art that each 1^0 C difference with the calculated Tm represents 1% mismatch (Sambrook et al, eds, 1989, Molecular Cloning, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, p.11.52, item 3). Thus "hybridizing at a temperature in the range of that from the Tm of a hybrid of completely matching nucleic acids to a temperature 20^0 C lower than the Tm" would allow hybridization of sequences that are at least 80% similar to SEQ ID NO:1, or a fragment thereof.

Studier teaches libraries of oligonucleotide primers of octamers, nonamers, or decamers, for use in random priming (column 16, last paragraph). The oligonucleotide taught by Studier et al would hybridize to the nucleotide sequence ranging from the 49th to 3,183rd bases of SEQ ID NO:1, under the hybridization conditions cited in claim 40.

Although the reference does not specifically teach that the primer hybridizes under stringent conditions with DNA having a nucleotide sequence ranging from the 49th to 3,183rd bases of SEQ ID NO:1, wherein the stringent conditions comprise a temperature in the range of that from the Tm of a hybrid of completely matching nucleic acids to a temperature 20^0 C lower

than the Tm, and the DNA encodes a protein specifically expressed in differentiated chondrocytes, however, the primer taught by the art would hybridize to a nucleotide sequence ranging from the 49th to 3,183rd bases of SEQ ID NO:1, wherein the stringent conditions comprise a temperature in the range of that from the Tm of a hybrid of completely matching nucleic acids to a temperature 20^{0} C lower than the Tm. The claimed DNA appears to be the same as the prior art oligonucleotide primer. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS
May 18, 2006

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER